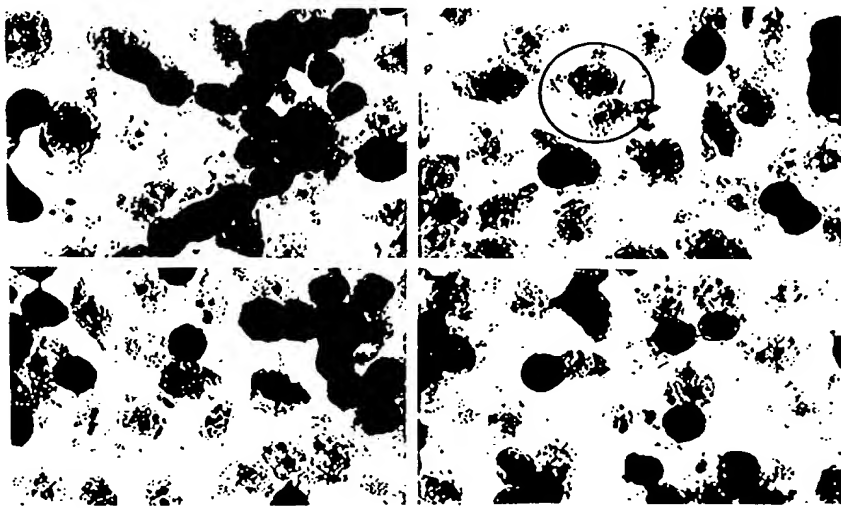


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|-----------|---|
| (51) International Patent Classification 6 : C12N 15/31, 15/62, C07K 14/22, 19/00, A61K 39/095 | A3 | (11) International Publication Number: WO 99/55875 (43) International Publication Date: 4 November 1999 (04.11.99) |
| (21) International Application Number: PCT/US99/09486 (22) International Filing Date: 29 April 1999 (29.04.99) (30) Priority Data: 60/083,405 29 April 1998 (29.04.98) US (71) Applicant (for all designated States except US): AMERICAN CYANAMID COMPANY [US/US]; Five Giralda Farms, Madison, NJ 07940 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): METCALF, Thomas, N., III [US/US]; 10 Caywood Lane, Fairport, NY 14450 (US). ZAGURSKY, Robert, J. [US/US]; 569 Fox Hunt Drive, Victor, NY 14564 (US). OOI, Peggy [US/US]; 494 Main Street Fishers, Mendon, NY 14506 (US). (74) Agents: GORDON, Alan, M.; American Home Products Corporation, Patent Law Dept. - 2B2, One Campus Drive, Parsippany, NJ 07054 (US) et al. | | (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 13 April 2000 (13.04.00) |
| (54) Title: VACCINES CONTAINING RECOMBINANT PILIN AGAINST <i>NEISSERIA GONORRHOEAE</i> OR <i>NEISSERIA MENINGITIDIS</i>  | | |
| (57) Abstract <p>The <i>pilE</i> genes of each of <i>Neisseria gonorrhoeae</i> and <i>Neisseria meningitidis</i> are cloned and their corresponding recombinant pilin proteins are expressed. In addition, a chimeric <i>pilE</i> gene is constructed in which the region of the <i>pilE</i> gene of <i>Neisseria meningitidis</i> class I encoding the amino-terminal region of the pilin protein is replaced by the corresponding region of the <i>pilE</i> gene of <i>Neisseria gonorrhoeae</i>. The recombinant meningococcal chimeric class I pilin protein is expressed at higher levels than the pilin protein expressed by the full-length <i>pilE</i> gene of <i>Neisseria meningitidis</i>. Furthermore, a chimeric <i>pilE</i> gene is constructed in which the region of the <i>pilE</i> gene of <i>Neisseria meningitidis</i> class II encoding the carboxy-terminal region of the pilin protein is replaced by the corresponding region of the <i>pilE</i> gene of <i>Neisseria gonorrhoeae</i>. The recombinant pilin proteins are used in vaccines to protect against disease caused by <i>Neisseria gonorrhoeae</i> or <i>Neisseria meningitidis</i>.</p> | | |

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INTERNATIONAL SEARCH REPORT

Inte Application No

PCT/US 99/09486

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/31 C12N15/62 C07K14/22 C07K19/00 A61K39/095

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 9-14, 29 and 30 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,15 (all partially); 2,7,8,9,13 (all completely)

A vaccine composition comprising isolated and purified recombinantly-expressed pilin protein from the species *Neisseria gonorrhoeae*, further comprising an adjuvant, diluent or carrier, the adjuvant being selected from the group consisting of aluminium hydroxide, aluminium phosphate, Stimulon QS-21, 3-O-deacylated monophosphoryl lipid A, Il-12, and wild-type or mutant cholera toxin, and methods of immunisation and preparation.

2. Claims: 1,3,10,12,15 (all partially); 4 (completely)

A vaccine composition comprising isolated and purified recombinantly-expressed class I pilin protein from the species *Neisseria meningitidis*, and methods of immunisation and preparation.

3. Claims: 1,3,10,12,15 (all partially); 5 (completely)

A vaccine composition comprising isolated and purified recombinantly-expressed class II pilin protein from the species *Neisseria meningitidis*, and methods of immunisation and preparation.

4. Claims: 1,15 (all partially); 6,11,14,
16-42 (all completely)

- A vaccine composition comprising isolated and purified recombinantly-expressed chimeric pilin protein of *Neisseria gonorrhoeae* and class I *Neisseria meningitidis* having the amino acid sequence 1-167 (or 8-167 after maturation) of SEQ ID NO:2 or a biologically equivalent amino acid sequence, and methods of immunisation and preparation.

Isolated and purified encoding nucleic acids and variants (SEQ ID NO:1), plasmids, host cells, methods of production, and the isolated and purified chimeric pilin.

- A vaccine composition comprising isolated and purified recombinantly-expressed chimeric pilin protein of *Neisseria gonorrhoeae* and class II *Neisseria meningitidis* having the amino acid sequence 1-170 (or 8-170 after maturation) of SEQ ID NO:4 or a biologically equivalent amino acid sequence, and methods of immunisation and preparation.

Isolated and purified encoding nucleic acids and variants (SEQ ID NO:3), plasmids, host cells, methods of production, and the isolated and purified chimeric pilin.

INTERNATIONAL SEARCH REPORT

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